

B! - cancelled
particles obtained by chopping the extruded filaments is directly spheroidal without any additional spheroidal shaping step.

REMARKS

New claims 7 and 8 were drafted to better distinguish over the reference cited as prior art by the Examiner.

Rejection under 35 U.S.C. §102

Now cancelled claims 5 and 6 are rejected under 35 U.S.C. 102(b), as being anticipated by WO 96/14058 to Oshlack et al. (hereinafter WO'058).

According to the Examiner, the disclosure of WO'058, i.e.

- the abstract,
- page 6, l. 13-30
- page 10, l. 21-26
- page 7, l. 15-30 and claim 18
- page 8, l. 1-2 and
- page 17, l. 23-25

"reads on the method of making particles as claimed by applicant"

That rejection is respectfully traversed.

First, the Examiner's attention is respectfully drawn to the fact that only claim 5 discloses a method of making particles.

And the rejection of claim 5 (amended) under 35 USC 102(b) as being anticipated by WO'58 is unfounded for the following raisons.

Even if, admittedly, WO'058 teaches a method which, according to the Examiner,

"... involves blending the drug with the matrix ingredients, heating the blended mixture, placing the mixture in the extruder, extruding the

strands, then dividing the strands into the desired pieces, such as pellets" (p. 7, l. 15-30, and claim 18).

W0'058 also teaches that

"... a water insoluble retardant, a therapeutically active agent and an optional binder..." (p.17, l.16) are *"... directly meter(ing)ed into an extruder..."* (p.17, l.15).

the *"homogeneous mixture"* (p.17, l.16 and 17) being heated and extruded.

On the contrary, according to new claim 7 the mixture in question is subjected to a heating step carried out outside the extruder at a temperature from 20 to 70°C which is maintained at least "30 minutes", advantageously in a ventilated tray type oven before being introduced into the extruding machine inside which it is heated to the extrusion temperature and subjected to the extrusion pressure during 2 to 6 minutes.

W0'058 does not disclose the heating step outside the extruder and therefore the rejection is not well founded.

Claim 8 discloses an apparatus for making particles in the form of spheroids said apparatus being characterized by the fact that it comprises a tool for chopping particles equipped with cutters as defined in claim 8 which permit obtaining particles which are directly spheroidal without an additional spheroidal shaping step.

On the contrary, W0'058 does not disclose an extruder comprising a tool for chopping particles equipped with cutters as defined in claim 6 and consequently the rejection of claim 6 under 35 USC 102 as being anticipated by W0'058 is not founded.

Rejection under 35 U.S.C. 103

Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over WP 96/14058 to Oshlack et al as applied to these claims above.

According to the Examiner

"... although W0'058 does not specifically refer to a maturing step, it is the position of the examiner that the heating step prior to extrusion, which is discussed by W0'058, reads on applicant's claimed maturing step."

and

"W0'058 does teach a heating step prior to the extrusion, and applicant's claimed maturing step is simply a heating step with a defined time and temperature."

and again

"there is no evidence that the prior art heating step is different than applicant's nor is there any evidence that there is a patentable difference between the resulting products."

That rejection is respectfully traversed.

The step disclosed by W0'058 and which according to the Examiner is a heating step is in fact consisting of the normal step carried out in an extrusion method during which the mixture to be extruded is brought to the extrusion temperature before extrusion proper, said "heating" step taking place within the extrusion machine, as appears for instance from Fig. 9 and from claim 18, i.e

"heating said blend to a temperature sufficient to soften the mixture sufficiently to extrude the same, extruding said heated mixture as a strand having a diameter of from 0.1 B 3 mm"

The duration of such a normal heating step actually corresponds to the time necessary to reach the intended extrusion temperature.

On the contrary the maturation step of the instant invention

- is carried out outside the extrusion machine and
- its duration is at least 30 minutes which is of course much longer than the

time necessary to heat the mixture to the extrusion temperature.

And nowhere in W0'058 there is the slightest suggestion to maintain at the extrusion temperature during at least 30 minutes before extruding the mixture to be extruded, once heated to the extrusion temperature.

And there was no reason for such a suggestion as W0'058 does not contemplate a storage longer than 6 hours of the mixture intended to be extruded, once it has been prepared.

In that connection the Examiner's attention is respectfully drawn to the instant specification from page 3, l. 26 to page 4, l. 20.

And in contradiction with the Examiner's statement there is evidence supporting patentable difference.

In that respect the Examiner's attention is respectfully drawn to examples 1 and 2 where the behavior of particles not having been subjected to the maturing heating step is compared with that of particles actually having been subjected to such a step.

These examples confirm the surprising and unexpected advantages obtained due to the maturing heating step, advantages which are recited from page 4, l.17 to page 5 l.5.

From the foregoing it clearly appears that the rejection under 35USC 103 of claim 7 in view of W0'058 is not founded.

Concerning the rejection under 35 USC 103 of now cancelled claim 6, applicant respectfully draws the Examiner's attention to the fact that W0'058 nowhere suggests

an extruder comprising a tool for shopping equipped with the cutters as defined in claim 6 which cutters permit obtaining spheroidal particles without any additional spheroidal shaping step.

Thus the apparatus according to claim 8 is not only novel but also unobvious over W0'058.

And the Examiner's comment, according to which

"[W0'058] by allowing the exit port of the extruder to be any shape so that the multiparticulates can be of any shape, this allows the exit port to be a shape that would form spheroidal particulates."

is not relevant as in any case W0'058 fails to teach how to shape the exit port of the extruder.

W0'058 merely indicates an alleged possibility without any indication permitting to put it into practice.

And even if admittedly, W0'058 had taught how to shape the exit port, that would not have rendered obvious the apparatus according to claim 8.

Thus the rejection of claim 6 under 35 USC 103 in view of W0'058 is not founded.

In view of the amended claim 5 and the foregoing remarks, it appears that the application is now in proper form and patentable over the prior art.

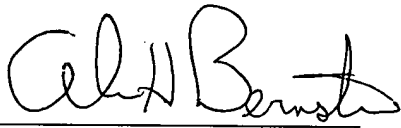
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Reconsideration and allowance are therefor respectfully solicited.

Respectfully submitted

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CLAIMS

Version with markings to show changes made

Please cancel claims 5 and 6.

Please add the following claim:

7. Method of making particles, in particular spheroids intended to be used for preparing tablets, said particles which include an active substance having a constant diameter in the range from 0.5 mm to 2 mm and a controlled and predetermined active substance release curve, said method including successively:

- a step of selecting an active substance and a thermoplastic material, including at least one polymer excipient and at least one plasticiser,

- a step of forming a mixture of the active substance and the thermoplastic material,

- a step of maintaining the mixture of the active substance and of the thermoplastic material at a temperature and for a time respectively selected in the range from 20 to 70°C and in the range from 30 minutes to 150 hours causing thus the maturing of the mixture, whereby it becomes possible to store the said mixture for up to 7 days before extruding it and to increase the quantity of active substance for a given release curve without increasing the volume of the tablet.

- a step of introducing the said mixture after maturing into the kneading area of an extruding machine,

- a step of extruding the said mixture, inside the extruding machine comprising a kneading area, without solvent at a controlled temperature to produce at least one extruded filament or extrudate and

- a step of chopping the extruded filament into particles

Please add the following claim:

8. Apparatus for making particles in the form of spheroids comprising a mixture of an active substance distributed within a thermoplastic material and having a constant diameter in the range from 0,5 to 2mm, said apparatus comprising an extruder which in turn comprises an extrusion die and which is proper to produce extruded filaments of said mixture, said apparatus further comprising, located at the exit of the extrusion die, a tool, for chopping the extruded filaments, wherein said tool is equipped with cutters in the form of blades having a first and second face parallel with one another, the first of which is inclined towards the second, thus forming a cutting edge, the second face being recessed so as to leave a strip of a whereby the shape of the particles obtained by chopping the extruded filaments is directly spheroidal without any additional spheroidal shaping step.

CERTIFICATE OF MAILING

I hereby certify that the foregoing AMENDMENT, re 09/402,564, is being deposited with the United States Postal Service, in duplicate, as First Class Mail, postage prepaid, in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, this 29th day of June 2001.

A handwritten signature in cursive script, appearing to read "Alan H. Bernstein", written over a horizontal line.

Alan H. Bernstein